1012-131 **Statins Decrease Mortality in Patients Undergoing Percutaneous Coronary Intervention With Left Ventricular Dysfunction**

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**Background**
While statins have been shown to decrease mortality in a population that went on to develop heart failure after beginning statin therapy, uncertainty remains whether statins are appropriate for patients with pre-existing left ventricular (LV) dysfunction. The goal of this study was to determine whether statin therapy improved survival in patients with LV dysfunction undergoing percutaneous coronary intervention (PCI).
**Methods**
We retrospectively evaluated consecutive patient procedures performed in our institution from 1996 through 1999. To be included, patients had to have a technically adequate angiographic LV gram with a calculated EF≤50%. Patients with prior CABG were excluded. Mortality data was retrieved using the United States Social Security Death Index. Follow-up ranged from 3.5 to 6.5 years.
**Data Analysis**
Cox Hazard regression, student T-tests, Kaplan-Meier survival analysis, and ROC curve analysis was performed to compare mortality and variables between the different subgroups. Means are provided with ± Std Dev and p-values less than 0.05 were considered significant.
**Results**
A total of 244 patients with an average EF of 39% ± 9.8% fulfilled our criteria. Mean age was 57.5 ±12 years, 68% were males, co-morbidities included 82% with HTN, 68% had hypercholesterolemia, and 36% had DM. Sixty-one percent underwent PCI for a recent MI, 68% percent of our population underwent PCI with stenting, and 64% were discharged on statins. During follow-up, 27% of our population died. Of the patients taking statins, 96% had hypercholesterolemia while 90% of patients with hypercholesterolemia were taking statins. Statins significantly improved survival at 1, 3, and 5 years (97% vs 84%, p<.001; 93% vs 72%, p<.00001; 87% vs 63%, p<.00001). Statin survival benefits persist regardless of MI history and EF. Statin use, along with age, calculated EF, diuretic use, and renal disease, was found to be significant on Cox Hazard Regression.
**Conclusion**.
In our retrospective analysis on patients with left ventricular dysfunction undergoing PCI, hypercholesterolemic patients discharged on statins had improved survival compared to patients not taking statins with normal cholesterol levels.

1012-132 **Atorvastatin Affects the Expression of Both Endothelium- and Liver-Derived Components of Thrombosis/Fibrinolysis System and Endothelial Function in Patients With Congestive Heart Failure**

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**Introduction:** Congestive heart failure (CHF) is characterised by endothelial dysfunction and increased thrombogenecity. We investigated the effect of atorvastatin on endothelial function and on plasma levels of antithrombin III (ATIII), proteins C and S, factors V and VII, von Willebrand factor (vWF), tissue plasminogen activator (tPA) and plasminogen activator inhibitor 1 (PAI-1) in patients with CHF.
**Methods:** Thirty-five patients with CHF (NYHA II-IV) were randomized to receive atorvastatin 10mg/day (n=17) or no statin (n=18) for 4 weeks. Forearm blood flow was measured by venous occlusion strain-gauge plethysmography. Endothelium dependent dilation (EDD) and endothelium independent dilation (EID) were expressed as the % change of flow from baseline to the maximum flow during reactive hyperemia or after sublingual nitroglycerin administration respectively. Plasma levels of thrombosis/fibrinolysis components were determined with ELISA.
**Results:** Atorvastatin improved EDD (42.44±4.5 to 83.7±8.5%, p<0.01), decreased plasma levels of tPA (15.5±2.2 to 12.3±1.6 ng/ml p<0.05), ATIII (82±3 to 74±4%, p<0.05), prtC (88±6 to 64±6%, p<0.01), fV (126±8 to 95±7%, p<0.01) and PAI-1 (3.02±0.39 to 1.96±0.34 IU/L, p<0.05), while it did not affect EID (65±8 to 53±6% p=ns) and levels of fVII (81±8 to 66±7% p=ns), vWF (135±13 to 123±19% p=ns) and prtS (93±5 to 95±8% p=ns). EDD and EID remained unchanged in controls (from 48±5 and 67±8 to 45±5% and 61±7% respectively p=ns for both). In control group, no significant change was observed in levels of ATIII (85±4 to 88±3%,p=ns), prtC(84±6 to 84±5%,p=ns), fV(131±10 to 122±9%,p=ns), fVII(78±12 to 69±9%,p=ns), vWF (151±19 to 135±38%, p=ns), prtS (100±8 to 96±6%, p=ns), tPA(13.2±1.5 to 11±2 ng/ml, p=ns) and PAI-1(2.64±0.38 to 3.25±0.34, p=ns).
**Conclusions:** Short-term treatment with atorvastatin improves endothelial function and reduces plasma levels of tPA, PAI-1, antithrombin III, protein C and factor V, in patients with CHF, suggesting that atorvastatin may affect the expression of both endothelium- and liver-derived components of thrombosis fibrinolysis system, beyond its effect on vascular endothelium in these patients.

1012-133 **Statin Therapy Can Improve Cardiac Function and Survival After Heart Failure in Rats**

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Background: Congestive heart failure has been shown to be related to an increase in oxidative stress. We hypothesized that statin, an inhibitor of 3-hydroxy-3-methylglutaryl-CoA reductase, prevents the progression from compensated left ventricular (LV) hypertrophy to heart failure and improves survival with a reduction in oxidative stress in a rat model. Methods and Results: Dahl salt-sensitive (DS) rats fed an 8% NaCl diet from 7 weeks of age were treated with pravastatin 50 mg/kg/day or 100 mg/kg/day from 7 or 12 weeks of age. At 18 weeks of age, untreated DS rats exhibited prominent concentric LV hypertrophy, and diastolic and systolic dysfunction was seen by echocardiography. We found that treatment with statin did not affect serum lipid levels or blood pressure. Treatment with pravastatin 100 mg/kg/day (but not 50 mg/kg/day) from 7 weeks of age attenuated hypertensive LV hypertrophy and markedly improved indices of diastolic function (peak negative myocardial velocity gradient); -2.25 ± 0.77/s to -3.28 ± 0.57/s, ($p < 0.05$) and systolic function (LV fractional shortening); 28.5 ± 1.5% to 35.2 ± 1.2%, ($p < 0.05$), and also improved survival rate (40.7% to 83.3%, $p < 0.01$). Treatment with statin ameliorated glutathione redox status ($p < 0.05$) and improved inflammatory responses. We also found that treatment with pravastatin (100 mg/kg/day only) from 12 weeks of age brought about the same benefit for cardiac function and survival. Conclusion: Statin therapy before and even after the development of hypertensive LV hypertrophy improved LV phenotypic changes, diastolic and systolic function, and survival in a rat hypertensive heart failure model.

1012-134 **Direct, Dose-Dependent Antifibrotic Effects of Atorvastatin in Human Cardiac Fibroblast Cell Culture**

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Background: HMGcoA reductase inhibitors (statins) may have beneficial effects on cardiac remodelling post myocardial injury. These effects appear to be additional to the lipid-lowering and anti-ischaemic actions of these agents. As pathological deposition of extracellular matrix (fibrosis) is a key component of remodelling post myocardial injury, we sought to determine whether these agents could directly inhibit matrix production *in-vitro,* as well as mechanisms by which these effects may occur.
**Methods:** The effect of atorvastatin (ATV, $10^{-8}$M-$10^{-5}$M) was examined in human cardiac fibroblast cell culture after stimulation with the known pro-fibrotic factors angiotensin II (AII, $10^{-7}$ M) and transforming growth factor-β (TGF-β). Non-stimulated, non-treated wells served as controls. Collagen production was estimated by [$^3$H]-proline incorporation (P).
**Results:** AII and TGF-β increased [$^3$H]-P by 38±17% and 90±34% respectively. ATV caused a dose-dependent reduction in [$^3$H]-P (% decrease c/f AII alone: $10^{-8}$M, -44±19%; $10^{-7}$M, -44±14%; $10^{-6}$M, -55±14%; $10^{-5}$M, -78±13%; p<0.05; % decrease c/f TGF-β alone: $10^{-8}$M, -9±4%; $10^{-7}$M, -20±12%; $10^{-6}$M, -46±6%; $10^{-5}$M, -67±15%; p<0.05). ATV similarly reduced AII- and TGF-β-induced [$^3$H]-P in a dose-dependent manner, p<0.05. Both AII and TGF-β significantly increased α(1) pro-collagen mRNA by 22 and 300% respectively; an effect that was blocked by ATV (% decrease c/f. AII alone: $10^{-5}$M: -54±23%; % decrease c/f TGF-β alone: $10^{-5}$M: -33±9.5%).
To determine whether these effects of statins were mediated by alterations in the pro-fibrotic peptide, connective tissue growth factor (CTGF), we measured CTGF mRNA in these studies. Both AII and TGF-β increased CTGF mRNA by 86±18% and 98±19% respectively; this was significantly reduced by ATV (% decrease c/f AII alone: $10^{-5}$M: -67%±18%; c/f TGF-β alone $10^{-5}$M: -44±13%).
**Conclusions:** We have demonstrated for the first time a direct, anti-fibrotic effect of statins in human cardiac fibroblast cell culture, following stimulation with pro-fibrotic factors known to be important in cardiac remodelling post-myocardial injury. These actions may contribute to the potential favourable anti-remodelling effects of statins.

POSTER SESSION

## 1013 Dilated Cardiomyopathy: Basic and Clinical I

Sunday, March 07, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1013-113 **Strain Rate and Strain Rate-Derived Time to Onset of Relaxation Can Be Used for the Early Detection of Impaired Myocardial Function in Asymptomatic Boys With Duchenne Muscular Dystrophy**

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Background. Patients with Duchenne muscular dystrophy (DMD) frequently develop dilated cardiomyopathy at the later stages of the disease. Strain rate (SR) has been used to study ischeamia and cardiomyopathies and time to onset of regional relaxation ($T_R$) by SR imaging has been used to quantify regional myocardial function. The aim of this study was to investigate the usefulness of SR and SR derived $T_R$ for the early detection of cardiac involvement in young, asymptomatic patients with DMD which is critical to initiate life-saving therapeutic interventions.